Photocyclizations of *N*-Chloroacetyltyramine. I. Formation of Novel Dimeric Cage Compounds[1]

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Received September 29, 1973

Abstract: Irradiation of *N*-chloroacetyltyramine (**1a**) in aqueous ethanol gave 8-hydroxy-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2-one (**2a**) and two novel dimeric cage compounds, decahydro-7,14a,7a,14-ethanediylidenenaphtho-[1,8-*de*:4,5-*d'e'*]bisazocine-4,6,11,13(1*H*,7*H*,8*H*,14*H*)-tetrone (**3a**, 40%) and dodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone (**4a**, 12%). *N*-Methyl (**1b**) and *N*-benzyl (**1c**) derivatives of **1a** gave similar results. Compound **3a** isomerized photochemically, not thermally, to **4a** in high yield. The homologous *N*-chloroacetyl-*p*-hydroxyphenylpropylamine (**16**) also gave a cage compound (**18**), whereas the lower homolog *N*-chloroacetyl-*p*-hydroxybenzylamine (**13**) rearranged to *p*-hydroxyacetanilide **15**. A plausible mechanism for the formation of **3a** and **4a** begins with formation of a cyclohexa-2,4-dienone which then undergoes a series of $(4_\pi + 2_\pi)$, $(2_\pi + 2_\pi)$, and $(_\sigma 2_a + _\sigma 2_a)$ cycloadditions.

Although the phenolic chromophore of *N*-chloroacetyltyrosine disappeared rapidly on photolysis in neutral and more so in alkaline solution, previous attempts to isolate homogeneous photoproducts were unsuccessful.[3] We have continued studies on these photoreactions in the tyramine series and have recently been successful in isolating novel cage dimers.

When a 7.5 m*M* solution of *N*-chloroacetyltyramine (**1a**) in 10% aqueous ethanol was irradiated for 1.5 hr with a 100-W high-pressure mercury lamp, the benzazepinone **2a** was isolated in 4.8% yield from the fraction soluble in ethyl acetate. The mass spectrum (M^+ 177) and elemental analysis indicate that **2a** has been formed with the loss of the elements of hydrogen chloride. The ir spectrum (amide 1648 cm^{-1}, no amide II band) proves that **2a** is a lactam with six or more, but less than nine, ring members.[4] The uv spectrum (λ_{max} at 282 nm) is indicative of an intact phenolic chromophore. Although the nmr spectrum shows the correct structure to be **2a**, and not **2a'**,[3] an unequivocal proof was provided by *O*-methylation of **2a** with diazomethane to the known compound **6a** prepared directly from *N*-chloroacetyl-*O*-methyltyramine (**5**)[5] (Scheme I).

From the aqueous layer the two dimeric cage compounds **3a** and **4a** were isolated in yields of 40 and 12%, respectively. Both **3a** and **4a**, on the basis of high-resolution mass spectra, have the composition $C_{20}H_{22}N_2O_4$ corresponding to dimers of **2a**. The ir spectra show them to be lactams with less than nine members because of the absence of amide II band.[4] The presence of the lactam rings was also confirmed by acid hydrolysis of **3a** to the amino acid derivative **7**.

The nmr spectra show that **3a** is a symmetrical dimer, while signals of **4a** with high field protons probably due to a cyclopropane ring are quite complicated. Neither **3a** nor **4a** shows signals due to vinyl protons, a strong indication that they must be cage-type molecules. In the uv spectra, both **3a** and **4a** have two ketonic groups each, because the molar extinction coefficients of their $n-\pi^*$ absorptions (**3a**, 300 nm; **4a**, 293.5 nm) are 102 and 104, respectively. The extinction of the *p*-bromophenylhydrazone of **3a**, 60,340, is about twice that of an ordinary ketone, such as the *p*-bromophenylhydrazone of acetone, λ_{max} 279 nm (ϵ 22,800).

Reduction of **3a** with sodium borohydride in aqueous methanol gave tetrahydro compound **8** which was also obtained by catalytic reduction with platinum oxide and which was characterized by spectral data and elemental analysis as an *N,N',O,O'*-tetraacetate.

Roentgen-ray analyses of **3b** and of the *N,N'*-diacetate of **4a** finally established the complete structures as decahydro-7,14a,7a,14-ethanediylidenenaphtho-[1,8-*de*:4,5-*d'e'*]bisazocine-4,6,11,13(1*H*,7*H*,8*H*,14*H*)-tetrone (**3b**) and dodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone (**4a**), respectively.[1,6] Figures 1 and 2 present the conformations and bond lengths.

The photolysis of the *N*-methyl homolog (**1b**) gave the same type of products, though their yields were not so good (**2b**, 1.5%; **3b**, 10.1%; **4b**, 1.3%). The *N*-benzyl derivative **1c** gave similar results.

The dimer **3a** rearranged photochemically, but not thermally, to **4a** in high yield, in a process which was irreversible. When **3a** in aqueous ethanol was irradiated (100-W high-pressure lamp, 12 hr), **4a** was isolated in 93% yield. However, both **3a** and **4a** were recovered unchanged after standing overnight at room temperature in 1 *N* hydrochloric acid or after heating for several hours in aqueous solution.

On the basis of the solvent effect studies[7] we proposed a dualistic mechanism, intramolecular transfer either of electrons or of energy, for the photoreactions of *N*-

(1) *Cf.* T. Iwakuma, H. Nakai, O. Yonemitsu, D. S. Jones, I. L. Karle, and B. Witkop, *J. Amer. Chem. Soc.*, 94, 5136 (1972); *cf.* IVth IUPAC Symposium on Photochemistry, Baden-Baden, July 1972, Abstracts, p 212.

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(3) O. Yonemitsu, T. Tokuyama, M. Chaykovsky, and B. Witkop, *J. Amer. Chem. Soc.*, 90, 776 (1968).

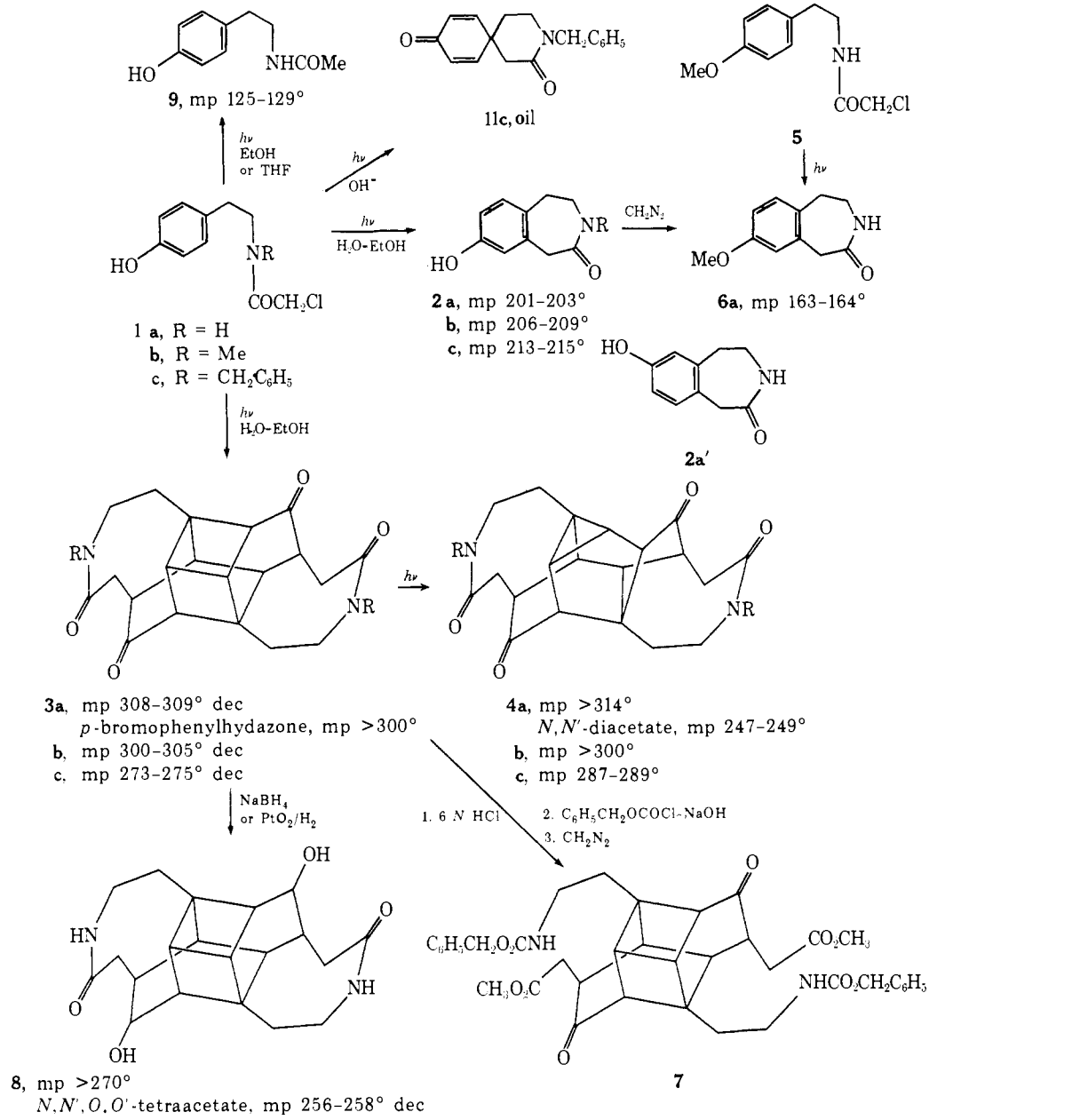
(4) R. Huisgen, H. Brade, H. Walz, and I. Glogger, *Chem. Ber.*, 90, 1437 (1957).

(5) H. Nakai, K. Hemmi, T. Iwakuma, and O. Yonemitsu, *Chem. Pharm. Bull.*, 20, 998 (1972).

(6) D. S. Jones and I. L. Karle, *Acta Crystallogr.*, in press.

(7) O. Yonemitsu, H. Nakai, Y. Okuno, S. Naruto, K. Hemmi, and B. Witkop, *Photochem. Photobiol.*, 15, 509 (1972).

Scheme I



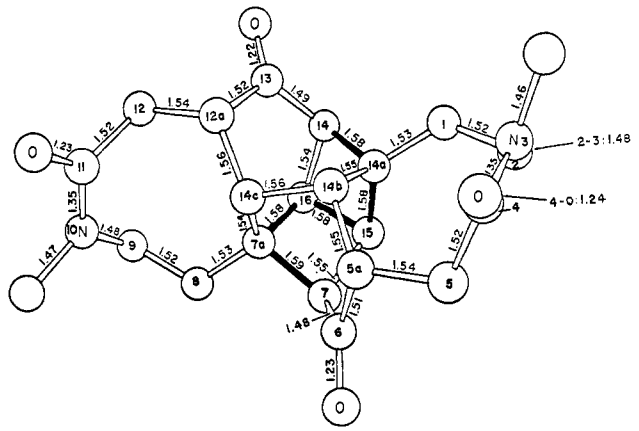


Figure 1. Correct name, numbering, and bond lengths of dimer **3b**, *i.e.*, decahydro-7,14a,7a,14-ethanediylidenenaphtho[1,8-*de*:4,5-*d'e'*]bisazocine-4,6,11,13-(1*H*,7*H*,8*H*,14*H*)-tetrone. The solid bonds of the two cyclobutane rings are unexpectedly long and undergo significant contraction on rearrangement to **4** when bonds 6–7 and 16–15 of **3b** switch to 8–15 and 7–7a in **4a**, respectively.

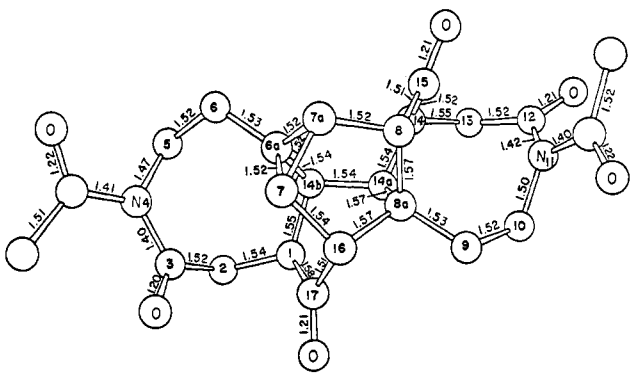


Figure 2. Correct name, numbering, and bond lengths of the *N,N'*-diacetate of dimer **4a**, 4,11-diacetyldodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone. In the meantime bond lengths of **3b** and **4a** have been refined (*cf.* ref **6**).

chloroacetylmescaline. As shown in Table I, products and yields in the photolysis of **1a** are also solvent

Scheme II

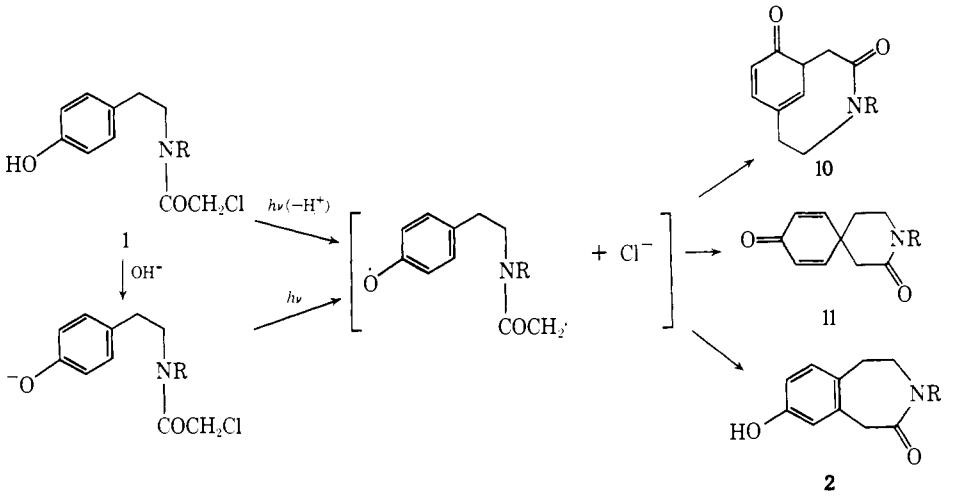


Table I. Effect of Solvent on Nature and Yield (%) of Photoproducts in the Photolysis of **1a**

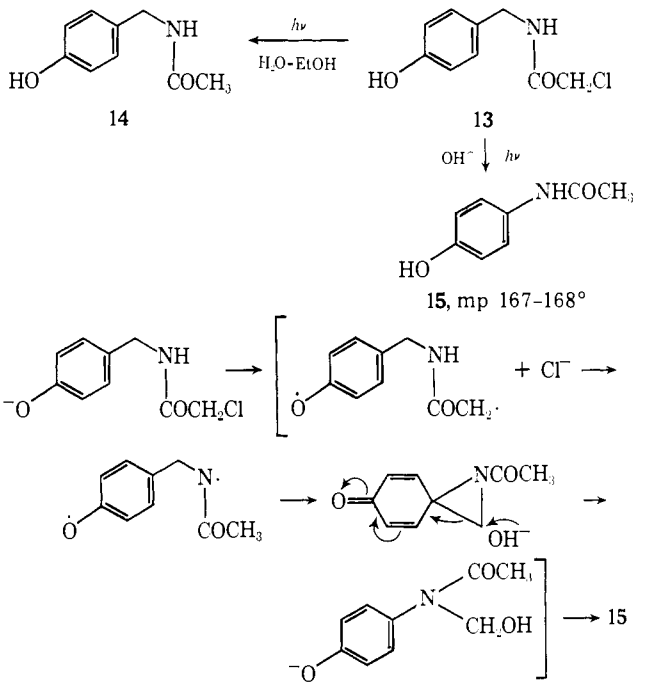
Solvent	Benzazepinone **2a**	*N*-Acetyltyramine **9**	Cage dimers **3a** + **4a**
H_2O–EtOH (9:1)	4.8		52.0
H_2O–EtOH (9:1) with NaOH (3 equiv)	3.2		40.0
H_2O–EtOH (9:1) with excess HCl	4.5		37.5
EtOH		6.3	Trace
Tetrahydrofuran		58.6	
Benzene			

dependent. In aqueous solution at both acidic, alkaline, as well as at neutral pH, **1a** was photolyzed to **2a** and dimers **3a** and **4a**. On the other hand, in hydrogen-donating solvents, especially in tetrahydrofuran, the reduction product *N*-acetyltyramine **9** became the single product, while in benzene most of the starting material was recovered.

Phenols on irradiation in aqueous solutions usually form the corresponding phenoxy radicals with ejection of an electron.[8] The photochemistry of phenols in such solutions is interpretable in terms of phenoxy radicals. Thus the formation of both **3a** and **4a** is best explained in terms of the key intermediate cyclohexa-2,4-dienone **10a** or cyclohexa-2,5-dienone **11a**, which in turn arise through the phenoxy radical intermediates of Scheme II, followed by cyclization of the biradical intermediates.[9]

We next examined the photoreactions of *N*-chloroacetyl-*p*-hydroxybenzylamine (**13**), which could form a cyclohexa-2,5-dienone, but not a cyclohexa-2,4-dienone, irrespective of any dimer formation. When **13** was irradiated in aqueous ethanol, *N*-acetyl-*p*-hydroxybenzylamine (**14**) was isolated as a single product with no traces of dimers. In alkaline solution *p*-hydroxyacetanilide (**15**) as well as **14** were isolated. Because neither light nor heat converted **14** to **15**, the mechanism of formation of the anilide **15** may be pictured as in Scheme III. This interesting series of reactions starts with the phenoxymethylene diradical, hydrogen abstraction from NH by the methylene radical, and the

Scheme III



formation of a spirodienone followed by alkaline hydrolysis to the anilide **15**. The photolysis of **13** in the presence of sodium borohydride again gave only **14**.

By contrast the homologous *N*-chloroacetyl-*p*-hydroxyphenylpropylamine (**16**) gave the benzazocinone **17** and the corresponding dimer **18** (Scheme IV). The structure of **17** was easily elucidated by analogy with that of the benzazepinone **2a** by uv, ir, nmr, and mass spectroscopy.[10] Dimer **18** with the composition $C_{22}H_{26}N_2O_4$ (mass spectrum) must be related to **3**, because its nmr signals appear quite symmetrical.

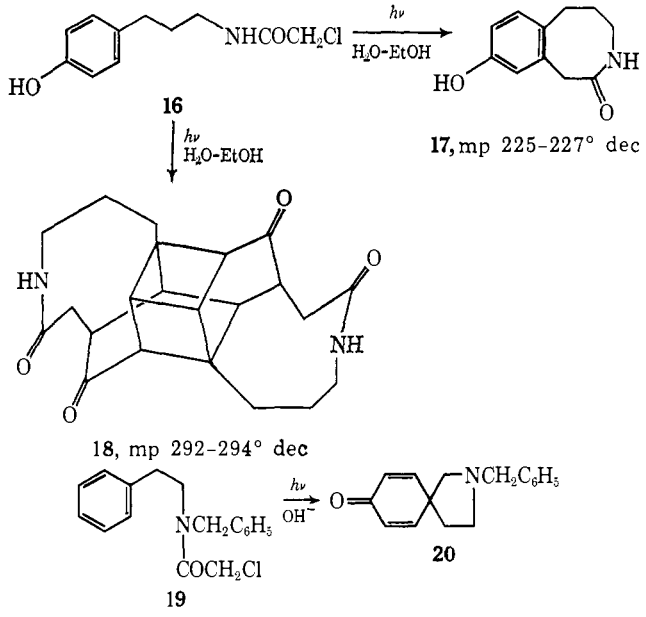
Further support for cyclohexadienones as transient intermediates was provided by isolation of a cyclohexa-2,5-dienone, which did not convert to dimers by further irradiation. When *N*-chloroacetyl-*N*-benzyl-*p*-hydroxybenzylamine (**19**) was irradiated in alkaline solution, the cyclohexa-2,5-dienone **20** was isolated in 11.2% yield. *N*-Chloroacetyl-*N*-benzyltyramine (**1c**) under the same conditions also gave the corresponding cyclohexa-2,5-dienone **11c**, though in low yield. On

(8) E. T. Land, G. Porter, and E. Strachan, *Trans. Faraday Soc.*, **57**, 1885 (1960); H.-I. Joschek and L. I. Grossweiner, *J. Amer. Chem. Soc.*, **88**, 3261 (1966).

(9) *Cf.* S. Naruto, O. Yonemitsu, N. Kanamaru, and K. Kimura, *J. Amer. Chem. Soc.*, **93**, 4053 (1971).

(10) *Cf.* Y. Okuno, K. Hemmi, and O. Yonemitsu, *Chem. Commun.*, 745 (1971).

Scheme IV



photolysis the isolated **11c** gave only tarry product. In spite of careful examination, no dimers were detected.

Flash photolysis of **1** afforded strong transient absorption spectra of cyclohexa-2,4-dienones as discussed in the following paper.[11]

The most probable mechanism for the formation of the remarkable cage dimers **3a** and **4a** may start with the formation of a cyclohexa-2,4-dienone, followed by a series of $[_\pi 4 + _\pi 2]$ and $[_\pi 2 + _\pi 2]$ cycloadditions,[12] and in the end, an unexpected bond switching process through Norrish type I cleavage or a novel cycloaddition $[_\sigma 2_a + _\sigma 2_a]$ (Scheme V). The final process probably proceeds in a concerted fashion, because it is neither influenced by triplet sensitizers, such as acetone, nor quenched by piperylene.

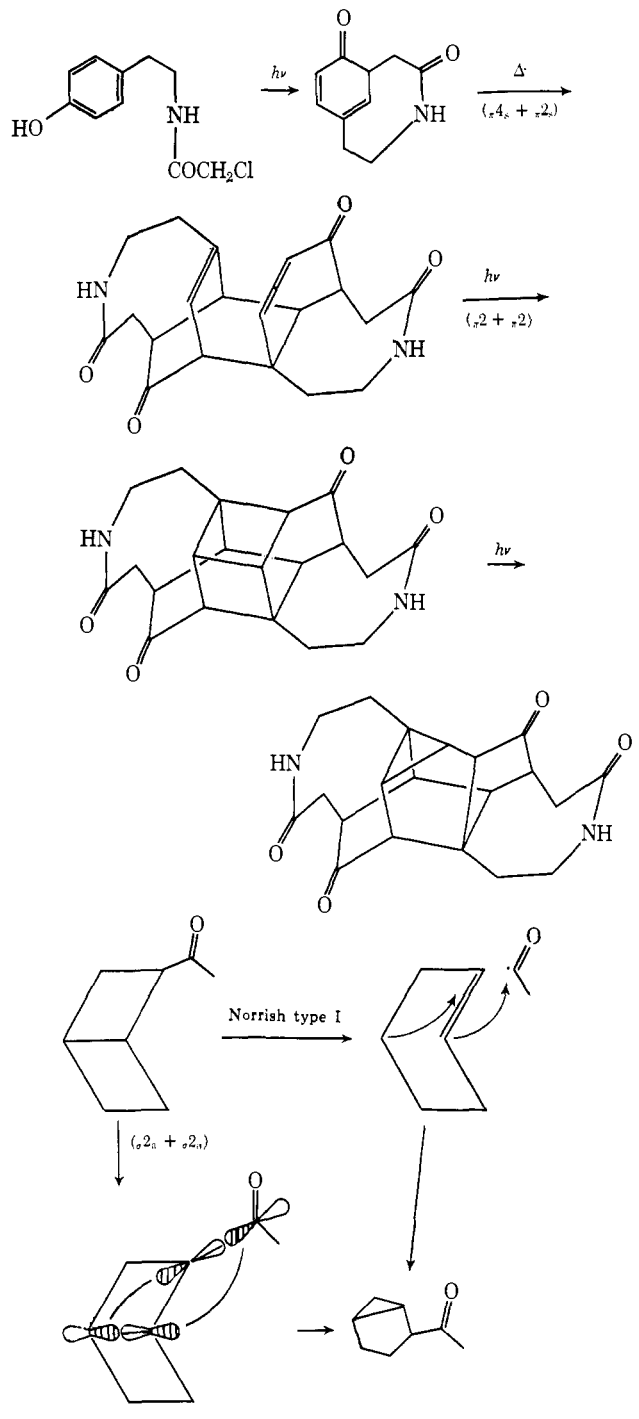
Experimental Section

N-Chloroacetyltyramines (**1a–c**). To a stirred solution of 10 mmol of tyramine, *N*-methyltyramine[13] or *N*-benzyltyramine[14] in 24 ml of 10% sodium hydroxide was added dropwise chloroacetyl chloride (15 mmol) over 5 min at 5–10°. The reaction mixture was stirred for 30 min at the same temperature, washed with benzene, and acidified by the addition of hydrochloric acid. The acidified solution was extracted with ethyl acetate; the extract was washed with water and dried over sodium sulfate. Evaporation of the solvent left the respective *N*-chloroacetyltyramine (**1a**, **1b**, or **1c**) in 40–50% yield (Table II).

N-Chloroacetyl-*p*-hydroxybenzylamines (**13**, **19**). *N*-Chloroacetyl-*p*-hydroxybenzylamine (**13**) and *N*-chloroacetyl-*N*-benzyl-*p*-hydroxybenzylamine (**19**) were synthesized from *p*-hydroxybenzylamine[15] and *N*-benzyl-*p*-hydroxybenzylamine[16] as described above (Table II).

N-Chloroacetyl-*p*-hydroxyphenylpropylamine (**16**). A solution of 10 mmol of *p*-methoxyphenylpropylamine[17] in 15 ml of 48% hydrobromic acid was heated under reflux for 3 hr. After evaporation of hydrobromic acid *in vacuo* the residue was treated with chloroacetyl chloride as described above to yield **16** (Table II).

Scheme V



Photolysis of *N*-Chloroacetyltyramine (**1a**). A solution of 1.0738 g (5.03 mmol) of *N*-chloroacetyltyramine (**1a**) in 750 ml of 10% aqueous ethanol was irradiated with a 100-W high-pressure mercury lamp (Eikosha) for 1.5 hr. The solution was stirred with excess silver carbonate to remove chloride ion, and the silver salts were removed by filtration over Celite. The filtrate was concentrated *in vacuo* to a volume of *ca.* 70 ml and extracted with ethyl acetate.

8-Hydroxy-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2-one (**2a**). The above ethyl acetate extract was dried over sodium sulfate and evaporated to leave 43 mg (4.8%) of **2a**. Recrystallization from acetone–*n*-hexane gave colorless prisms: mp 201–203°; uv λ_{max} (EtOH) 282 nm (ϵ 1960); ir (Nujol) ν 3200–3300 and 1648 cm^{-1}; mass spectrum *m/e* 177 (M^+), 148, 133, 121, and 120; nmr (DMSO-d_6) δ 2.82 (t, 2 H, J = 7 Hz), 3.50 (t, 2 H, J = 7 Hz), 3.58 (s, 2 H), 6.48 (d, 1 H, J = 2 Hz), 6.55 (q, 1 H, J = 2 and 8 Hz), 6.90 (d, 1 H, J = 8 Hz), 7.45 (broad s, 1 H), and 9.13 (s, 1 H).

Dodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa-

(11) T. Iwakuma, K. Hirao, and O. Yonemitsu, *J. Amer. Chem. Soc.*, **96**, 2570 (1974).

(12) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim/Bergstr., Germany, 1970, p 65.

(13) T. Sugama and S. Kanao, *Yakugaku Zasshi*, 84, 1014 (1964).

(14) F. Hoffmann-La Roche & Co., German Patent 259874 (1912); *Chem. Abstr.*, 7, 3198[1] (1913).

(15) G. Martinesco and M. Tiffeneau, *C. R. Soc. Biol.*, 73, 301 (1913).

(16) H. R. Snyder and J. R. Demuth, *J. Amer. Chem. Soc.*, 78, 1981 (1956).

(17) A. W. Fort and J. D. Roberts, *J. Amer. Chem. Soc.*, 78, 584 (1956).

Table II. Properties of *N*-Chloroacetyl Derivatives (1a, 1b, 1c, 13, 16, and 19)

Compd	Mp, °C	Appearance (recrystn solvent)	Uv_{max}^{EtOH}, nm (ε)	Ir, ν, cm^{-1}	Mass *m/e* M^+
1a	107–109	Prisms (EtOAc)	275[a] (1620)	3400 1600	213
1b	154–156	Prisms (EtOAc)	280 (1950)	3240 1642	227
1c	119–121	Prisms (EtOAc–hexane)	280 (1830)	3140 1630	303
13	117–119	Needles (EtOAc–benzene)	279 (1688)	3310 1642	199
16	88–89	Prisms (EtOAc–benzene)	280 (1885)	3200 1650	227
19	117–119	Prisms (Benzene)	279 (1476)	3250 1630	289

[a] Solvent, 10% aqueous ethanol.

[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone (4a). The aqueous layer after extraction of **2a** was evaporated *in vacuo* to dryness; the residue was washed with 10 ml of methanol and then stirred in 15 ml of water for 15 min. The insoluble crystals of **4a** collected by filtration weighed 107 mg (12%). Recrystallization from methanol–water gave colorless prisms: mp 314°; uv λ_{max} (H_2O) 293.5 nm (ε 46); ir (Nujol) ν 3200–3380, 1720, 1680, and 1650 cm^{-1}; mass spectrum *m/e* 354 (M^+).

Decahydro-7,14a,7a,14-ethanediylidenenaphtho[1,8-*de*:4,5-*d'e'*]-bisazocine-4,6,11,13(1*H*,7*H*,8*H*,14*H*)-tetrone (3a). After separation of **4a** the aqueous mother liquor was evaporated *in vacuo* to leave 356 mg (40.0%) of **3a**. Recrystallization from small amounts of water gave colorless needles: mp 308–309° dec; uv λ_{max} (H_2O) 195 nm (ε 14,400) and 300 (102); ir (Nujol) ν 3560, 3440, 3300, 1718, 1695, and 1660 cm^{-1}; mass spectrum *m/e* 354 (M^+), 325, and 296; nmr (D_2O) δ 1.56–1.84 (m, 2 H), 1.92–2.24 (m, 2 H), 2.34 (d, 2 H, *J* = 3.5 Hz), 2.84 (d, 2 H, *J* = 4 Hz), 3.00 (q, 2 H, *J* = 3.5 and 8.5 Hz), 3.12 (d, 2 H, *J* = 4 Hz), and 3.20–3.48 (m, 4 H).

***p*-Bromophenylhydrazone of 3a.** An 80% aqueous ethanol solution of 145.2 mg (0.4 mmol) of **3a** and 187 mg (1.0 mmol) of *p*-bromophenylhydrazine was heated under reflux for 6 hr. After cooling, the pale yellow prisms were collected by filtration: 166.1 mg (60%), mp 300°; uv λ_{max} (EtOH) 293.5 nm (ε 60,340); ir (Nujol) ν 3290, 1675, and 1590 cm^{-1}.

4,11-Diacetyldodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone. When a solution of **4a** (35.4 mg, 0.1 mmol) in 5 ml of acetic anhydride was heated under reflux for 1.5 hr, the residue, after evaporation of the acetic anhydride, was triturated with 10 ml of ether to afford 35.4 mg (80.8%) of a colorless crystalline powder. Recrystallization from 50% methanol afforded colorless prisms: mp 247–249°; ir ($CHCl_3$) ν 1740 and 1700 cm^{-1}; mass spectrum *m/e* 438 (M^+), 396, 378, 298, and 256; nmr ($CDCl_3$) δ 2.40 (s, 3 H) and 2.52 (s, 3 H).

8-Methoxy-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2-one (6a). An ether solution of excess diazomethane was added to a solution of 3 mg of **2a** in 3 ml of methanol–tetrahydrofuran (1:1), and allowed to stand overnight. Evaporation of the solvents left colorless crystals, mp 163–164°, identical with an authentic sample[5] by the criteria of ir, mass spectra, tlc, and mixture melting point.

Acid Hydrolysis of 3a. A 6 *N* hydrochloric acid (24 ml) solution of 400 mg (1.13 mmol) of **3a** was heated under reflux for 4 hr. After removal of the hydrochloric acid *in vacuo*, the residue was dissolved in 10 ml of 5% sodium hydroxide solution, and to the stirred solution was added dropwise 840 mg (4.9 mmol) of carbobenzoxy chloride at 5–10°. The stirring was continued for 1 hr at room temperature; the reaction mixture was washed with chloroform, acidified by the addition 5% hydrochloric acid, and extracted with chloroform. The extract was dried over sodium sulfate and the solvent was evaporated to leave 300 mg of a tan residue, which was dissolved in 30 ml of tetrahydrofuran and treated with an ether solution of excess diazomethane overnight at room temperature. After evaporation of the solvents, the residue was chromatographed on an alumina column (30 g). Elution with chloroform gave 125 mg (16.1%) of a pale yellow syrup of **7**: ir ($CHCl_3$) ν 3550 and 1740 (broad) cm^{-1}; mass spectrum *m/e* 686 (M^+), 536, 444, 400, and 342; nmr ($CDCl_3$) δ 3.68 (s, 6 H), 5.09 (s, 4 H), and 7.31 (s, 10 H).

Reduction of 3a. A. With Sodium Borohydride. To a 33% aqueous methanol solution of 300 mg (0.85 mmol) of **3a** was added 100 mg (2.64 mmol) of sodium borohydride at 0–5°, and the mixture was stirred for 3 hr at room temperature. After neutralization by the addition of 10% hydrochloric acid, the solution was concentrated *in vacuo* and the dried residue was extracted with methanol. The methanol solution was evaporated to leave colorless crystals, which were stirred in 10 ml of ethanol for 30 min. The remaining insoluble crystals were collected by filtration, 182 mg (60.0%). Recrystallization from water gave colorless prisms of **8**: mp 270°; ir (Nujol) ν 3200–3600 and 1650 cm^{-1}.

B. Catalytic Reduction with Platinum Oxide. A 50% aqueous methanol solution (25 ml) of 100 mg (0.28 mmol) of **3a** was shaken under 3 atm of hydrogen in the presence of 100 mg of PtO_2 catalyst at room temperature for 12 hr. After removal of the catalyst by filtration, the filtrate was evaporated to dryness, and the residue was recrystallized from water to give 70.5 mg (70%) of colorless prisms of **8**, mp 270°.

Tetraacetate of 8. A solution of 50 mg (0.14 mmol) of **8** in 15 ml of acetic anhydride was heated under reflux for 2 hr. After evaporation of the acetic anhydride, the residue was recrystallized from 1-butanol to give 58.7 mg (80%) of colorless needles: mp 256–258° dec; ir (Nujol) ν 1732 and 1700 cm^{-1}; mass spectrum *m/e* 526 (M^+), 466, 424, and 408; nmr ($CDCl_3$) δ 2.00 (s, 6 H), 2.45 (s, 6 H), and 4.58 (d, 2 H, *J* = 1.5 Hz).

Photolysis of *N*-Chloroacetyl-*N*-methyltyramine (1b). A solution of 2.8 g (12.3 mmol) of **1b** in 800 ml of 25% aqueous ethanol was irradiated with a 200-W high-pressure mercury lamp for 2 hr. The solution was treated with excess silver carbonate and the silver salts were removed by filtration. The filtrate was concentrated *in vacuo* to a volume of *ca.* 50 ml and extracted with ethyl acetate.

8-Hydroxy-3-methyl-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2-one (2b). The ethyl acetate extract was dried over sodium sulfate and evaporated to give yellow crystals of **2b**. Recrystallization from methanol gave 35.2 mg (1.5%) of colorless prisms: mp 206–209°; uv λ_{max} (EtOH) 282 nm (ε 1960); ir (Nujol) ν 3120 (broad), 1630, and 1600 cm^{-1}; mass spectrum *m/e* 191 (M^+) and 120.

Decahydro-3,10-dimethyl-7,14a,7a,14-ethanediylidenenaphtho[1,8-*de*:4,5-*d'e'*]bisazocine-4,6,11,13(1*H*,7*H*,8*H*,14*H*)-tetrone (3b). The aqueous layer was evaporated *in vacuo* to leave a brown oil, which was chromatographed on alumina. Elution with chloroform gave a colorless solid of a mixture of **3b** and **4b**, which was recrystallized from methanol to yield 238 mg (10.1%) of **3b** as colorless prisms: mp 300–305° dec; uv λ_{max} (H_2O) 297 nm (ε 164); ir (Nujol) ν 1702 and 1640 cm^{-1}; mass spectrum *m/e* 382 (M^+), 354, 339, 327, 311, and 298; nmr (D_2O) δ at 70° 1.60–1.92 (m, 2 H), 2.08–2.40 (m, 2 H), 2.25 (s, 2 H), 2.92 (s, 6 H), and 3.56 (t, 4 H, *J* = 6 Hz).

4,11-Dimethyldodecahydro-7*H*-1,7,8a-ethanylylidene-8,14-methanocyclopropa[1,6]benzo[1,2-*d*:4,3-*d'*]bisazocine-3,12,15,17(4*H*,9*H*)-tetrone (4b). The mother liquor after recrystallization of **3b** was purified by silica gel tlc (ethyl acetate–methanol = 1:1) to give 33 mg (1.3%) of **4b**. Recrystallization from ethyl acetate–methanol gave a colorless microcrystalline powder: mp 300°; ir (Nujol) ν 3400, 1740, 1708, and 1632 cm^{-1}; mass spectrum *m/e* 382 (M^+), 368, 339, 308, and 283.

Photolysis of *N*-Chloroacetyl-*N*-benzyltyramine (1c). A solution of 894 mg (3 mmol) of **1c** in 400 ml of 30% aqueous ethanol was irradiated with a 100-W high-pressure lamp for 5 hr. The chloride ion was removed by the addition of silver carbonate; the filtrate was concentrated *in vacuo* to a volume of *ca.* 50 ml and extracted with ethyl acetate. The extract was dried over sodium sulfate and evaporated to leave 510 mg of a dark oil, which was chromatographed on a column of 30 g of alumina. Elution with chloroform gave a mixture of **3c** and **4c**, which was separated by tlc (silica gel, ethyl acetate–methanol 15:1). From the lower fraction 57 mg (7.1%) of **3c** was isolated and recrystallized from methanol to give colorless prisms: mp 273–275° dec; uv λ_{max} (MeOH) 305 nm (ε 117.5); ir (Nujol) ν 1700 and 1640 cm^{-1}; mass spectrum *m/e* 534 (M^+), 506, 478, 443, 415, and 386; nmr ($CDCl_3$) δ at 60° 4.36 (d, 2 H, *J* = 14 Hz), 4.75 (d, 2 H, *J* = 14 Hz), and 7.25 (s, 10 H).

From the upper fraction, 20 mg (2.5%) of **4c** was isolated and recrystallized from methanol to give colorless needles: mp 287–289°; ir ($CHCl_3$) ν 1735, 1720, and 1635 cm^{-1}; mass spectrum *m/e* 534 (M^+), 506, 478, 415, and 387.

The above alumina column was eluted with chloroform–methanol (9:1) to give 15.3 mg (2.0%) of **2c**, which was recrystallized from methanol to give colorless prisms: mp 213–215°; ir (Nujol) ν 3150 and 1635 cm^{-1}; uv λ_{max} (MeOH) 282 nm (ε 1930); mass spectrum

m/e 267 (M^+), 120, and 91; nmr ($CDCl_3$) δ 2.88 (t, 2 H, J = 7 Hz), 3.62 (t, 2 H, J = 7 Hz), 3.90 (s, 2 H), 4.60 (s, 2 H), 6.66 (d, 1 H, J = 2 Hz), 6.70 (q, 1 H, J = 2 and 8 Hz), 6.91 (d, 1 H, J = 8 Hz), and 7.24 (s, 5 H).

Photochemical Conversion of 3a to 4a. Dimer **3a** (21.5 mg) was dissolved in 10% aqueous ethanol and irradiated with a 100-W high-pressure lamp (external irradiation) for 12 hr. After evaporation of the solvent, the residue was triturated with ether to give 20.0 mg (93.1%) of colorless crystals of **4a**. A similar irradiation of **3a** in a Pyrex cell for 20 hr also gave **4a** in 76% yield.

Photolysis of 1a in Various Solvents. Solutions of 213 mg (1 mmol) of **1a** in 150 mg of 10% aqueous ethanol containing 168 mg (3 mmol) of potassium hydroxide, 10% aqueous ethanol containing 6 *N* hydrochloric acid (60 mmol), ethanol, tetrahydrofuran, or benzene were irradiated with a 100-W lamp for 1.5 hr. Each reaction mixture was worked up as described above. The ethyl acetate extract was chromatographed on silica gel tlc (ethyl acetate) or on a silica gel column (ethyl acetate–hexane = 1:1) to give recovered starting material **1a**, benzazepinone **2a**, and *N*-acetyltyramine.[18] From the aqueous layers **3a** and **4a** were isolated. The results are summarized in Table I.

Photolysis of *N*-Chloroacetyl-*p*-hydroxybenzylamine (13). A. In Aqueous Ethanol. A solution of 597 mg (3 mmol) of **13** in 300 ml of 10% aqueous ethanol was irradiated with a 100-W high-pressure lamp for 8 hr. After treatment with silver carbonate, the filtrate was concentrated to a volume of 50 ml and extracted with ethyl acetate, and the extract was dried over sodium sulfate and evaporated to leave an oil, which was purified on silica gel tlc (ethyl acetate) to give 100 mg (20.2%) of *N*-acetyl-*p*-hydroxybenzylamine (**14**). Recrystallization from benzene–ethyl acetate gave colorless prisms: mp 132–334°;[19] ir (Nujol) ν 3420 and 1640 cm^{-1}; mass spectrum *m/e* 165 (M^+), 122, and 107; nmr ($CDCl_3$, CF_3COOH) δ 2.40 (s, 3 H), 4.55 (s, 2 H), 6.50 (d, 2 H, J = 9 Hz), 7.20 (d, 2 H, J = 9 Hz).

B. In Aqueous Potassium Hydroxide. Compound **13** (597 mg) in 300 ml of water containing 504 mg (9 mmol) of potassium hydroxide was irradiated with the same lamp for 3 hr. The solution was neutralized by the addition of 10% hydrochloric acid, and extracted with ethyl acetate. The extract was dried and evaporated to give an oil, which was separated on silica gel tlc (ethyl acetate) to give 88 mg (17.7%) of **14** and 40 mg (8.8%) of 4-hydroxyacetanilide (**15**). Recrystallization from benzene–ethyl acetate gave colorless prisms: mp 167–168°;[20] ir (Nujol) ν 3350, 3150, and 1650 cm^{-1}; mass spectrum *m/e* 151 (M^+) and 109; nmr (DMSO-d_6) δ 1.93 (s, 3 H), 6.61 (d, 2 H, J = 9 Hz), and 7.30 (d, 2 H, J = 9 Hz).

C. In Aqueous Potassium Hydroxide Containing Sodium Borohydride. Compound **17** was irradiated as in the preceding experiment in the presence of 334 mg (9 mmol) of sodium borohydride. The ethyl acetate extract was chromatographed on alumina (2.0 g) and eluted with ethyl acetate–methanol (9:1) to give 241 mg (48%) of **14**.

Photolysis of *N*-Chloroacetyl-3-(*p*-hydroxyphenyl)propylamine (16). A solution of 1.135 g (5 mmol) of **16** in 500 ml of 10% aqueous ethanol was irradiated with a 60-W low-pressure lamp (Eikosha) for 4 hr. After removal of chloride ion by the addition of silver carbonate, the filtrate was evaporated *in vacuo* to dryness. The residue was decolorized by activated charcoal in 500 ml of ethanol. The charcoal was removed by filtration and the filtrate evaporated to leave an oil, which was chromatographed on a column of silica gel (25 g).

9-Hydroxy-1,2,3,4,5,6-hexahydro-3-benzazocin-2-one (17). Elution with ethyl acetate afforded 23.8 mg (2.5%) of **17**, which was recrystallized from ethanol to give colorless needles: mp 255–257° dec; uv λ_{max} (EtOH) 284 nm (ϵ 2070); ir (Nujol) ν 3280, 3180, 1662, and 1605 cm^{-1}; mass spectrum *m/e* 191 (M^+), 174, 152, 121, 120, and 107; nmr (DMSO-d_6, $CDCl_3$) δ 1.3–2.0 (m, 2 H), 2.65–2.95 (m, 2 H), 3.00–3.20 (m, 4 H), 6.51 (q, 1 H, J = 8 and 2 Hz), 6.67 (d, 1 H, J = 2 Hz), and 6.88 (d, 1 H, J = 8 Hz).

Dimer 18. Further elution with ethyl acetate–methanol (2:1) afforded a tan product which was rechromatographed over alumina (20 g) and eluted with ethyl acetate–methanol (7:1) to give 28.6 g (3.0%) of **18**. Recrystallization from ethanol afforded colorless prisms: mp 292–294° dec; ir (Nujol) ν 3450, 3200, 1706, and 1665 cm^{-1}; mass spectrum *m/e* 382 (M^+), 354, 310, 191, and 136.

Photolysis of *N*-Chloroacetyl-*N*-benzyl-*p*-hydroxybenzylamine (19). A solution of 1.445 g (5 mmol) of **19** in 500 ml of water containing 2.8 g (50 mmol) of potassium hydroxide was irradiated with a 100-W lamp for 4 hr. The solution was extracted with ethyl acetate; the extract was dried, evaporated, and chromatographed on alumina. Elution with ethyl acetate gave 142 mg (11.2%) of a cyclohexa-2,5-dienone, **20**, which was recrystallized from benzene to give colorless prisms: mp 122–125°; uv λ_{max}(EtOH) 237.5 nm (ϵ 14860); ir (Nujol) ν 1675 and 1663 cm^{-1}; mass spectrum *m/e* 253 (M^+), 196, 146, 134, 120, and 91; nmr ($CDCl_3$) δ 2.60 (s, 2 H), 3.28 (s, 2 H), 4.49 (s, 2 H), 6.23 (d, 2 H, J = 10 Hz), 6.83 (d, 2 H, J = 10 Hz), and 7.30 (s, 5 H).

Photolysis of 1c in Alkaline Medium. A solution of 1.22 g (4 mmol) of **1c** in 400 ml of water containing 2.24 g (40 mmol) of potassium hydroxide was irradiated with a 100-W lamp for 3.5 hr. After neutralization with acetic acid, the solution was extracted with ethyl acetate. The extract was dried, evaporated, and chromatographed on a column of alumina (50 g) to give three fractions, A, B, and C.

Fraction A, eluted with ethyl acetate–*n*-hexane, was rechromatographed on silica gel tlc (ethyl acetate–*n*-hexane 1:1) to afford 19.4 mg (1.8%) of the cyclohexa-2,5-dienone **11c** as a colorless oil: uv λ_{max}(EtOH) 232 nm (ϵ 18,600); ir (Nujol) ν 1662, 1642, and 1630 cm^{-1}; mass spectrum *m/e* 267 (M^+), 160, 120, 118, and 91; nmr ($CDCl_3$) δ 1.90 (t, 2 H, J = 7 Hz), 2.50 (s, 2 H), 3.40 (t, 2 H, J = 7 Hz), 4.70 (s, 2 H), 6.25 (d, 2 H, J = 11 Hz), and 6.82 (d, 2 H, J = 11 Hz).

Fraction B, eluted with chloroform, was rechromatographed on silica gel tlc (ethyl acetate–methanol 15:1) to give 84 mg (7.8%) of **3c** and 5.6 mg (0.5%) of **4c**.

Fraction C, eluted with chloroform–methanol (9:1), was purified on silica gel tlc (ethyl acetate–*n*-hexane 2:1) to afford 10 mg (0.9%) of **2c**.

Acknowledgment. The financial support of this work by the Ministry of Education of Japan is gratefully acknowledged.

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